

What is claimed:

1. A method of treating or ameliorating an indication of the invention in an animal, including a human, comprising administering an effective amount of (A) a compound of formula (I):



wherein:

- a. Ar is a five or six membered heteroaryl ring having a first ring nitrogen and optionally second or third ring nitrogens, with the remaining ring atoms being carbon, oxygen, or sulfur, provided the first nitrogen of Ar is a quaternary nitrogen and Ar is not thiazolium, oxazolium or imidazolium;
- b. Y is substituted on the first ring nitrogen, with the proviso that if Ar is pyrazole, indazole, (1,2,3)-triazole, benzotriazole, or (1,2,4)-triazole, the second ring nitrogen is substituted with
  1. alkyl or alkoxycarbonylalkylene;
  2. Ar\* {wherein, consistent with the rules of aromaticity, Ar\* is C<sub>6</sub> or C<sub>10</sub> aryl or a 5- or 6-membered heteroaryl ring, wherein 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring may be fused to a benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar\*)}; or
  3. Ar\*alkyl-, Ar\*C(O)alkyl-, Ar\*sulfonylalkyl-, or Ar\*sulfinylalkyl-; and
- c. Ar can be substituted on ring carbon atoms
  1. with one or more substituents independently selected from the group consisting ω-alkylenesulfonic acid, carbamoyl, Ar\*, Ar\*-alkyl-, Ar\*-O-, Ar\*SO<sub>2</sub>-, Ar\*SO-, Ar\*S-, Ar\*SO<sub>2</sub>NH-, Ar\*NH, (N-Ar\*)(N-alkyl)N-, Ar\*C(O)-, Ar\*C(O)NH-, Ar\*NH-C(O)-, and (N-Ar\*)(N-alkyl)N-C(O)-; or
  2. two adjacent substitutions together with their ring carbons form a C<sub>6</sub>- or C<sub>10</sub>-aromatic fused ring system; or
  3. two adjacent substitutions together with their ring carbons form a C<sub>5</sub>-C<sub>7</sub> fused cycloalkyl ring having up to two double bonds including the fused double

bond of the Ar group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. two adjacent substitutions together with their ring carbons form a fused five to eight membered heterocycle, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and  $S(O)_n$ , wherein  $n=0,1$ , or  $2$ ; or
5. two adjacent substitutions together with their ring carbons form a fused five or six membered heteroaryl ring, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the fused heteroaryl ring consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and sulfur;

d. Y is:

1. a group of the formula  $-CH(R^5)-R^6$

(a)  $R^5$  is hydrogen, alkyl-, cycloalkyl-, alkenyl-, alkynyl-, aminoalkyl-, hydroxy[ $C_1$  to  $C_6$ ]alkyl, dialkylaminoalkyl-, (N-[ $C_6$  or  $C_{10}$ ]aryl)(N-alkyl)aminoalkyl-, piperidin-1-ylalkyl-, pyrrolidin-1-ylalkyl, azetidinyllalkyl, 4-alkylpiperazin-1-ylalkyl, 4-alkylpiperidin-1-ylalkyl, 4-[ $C_6$  or  $C_{10}$ ]arylpiperazin-1-ylalkyl, 4-[ $C_6$  or  $C_{10}$ ]arylpiperidin-1-ylalkyl, azetidin-1-ylalkyl, morpholin-4-ylalkyl, thiomorpholin-4-ylalkyl, piperazin-1-ylalkyl, piperidin-1-ylalkyl, [ $C_6$  or  $C_{10}$ ]aryl, or independently the same as  $R^6$ ;

(b) wherein  $R^6$  is

- (1) hydrogen, alkyl (which may be substituted by alkoxycarbonyl)-, alkenyl, alkynyl, cyano-, cyanoalkyl-, or  $R_s$ , wherein  $R_s$  is a [ $C_6$  or  $C_{10}$ ]aryl or a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or
- (2) a group of the formula  $-W-R^7$ , wherein  $R^7$  is alkyl, alkoxy, hydroxy, or  $R_s$ , wherein W is  $-C(=O)-$  or  $-S(O)_2-$ ;
- (3) a group of the formula  $-W-OR^8$  wherein  $R^8$  is hydrogen or alkyl,
- (4) a group of the formula  $-CH(OH)R_s$ ; or

(5) a group of the formula  $-W-N(R^9)R^{10}$ , wherein

(a)  $R^9$  is hydrogen and  $R^{10}$  is an alkyl or cycloalkyl, optionally substituted by

(i)  $[C_6 \text{ or } C_{10}]$ aryl, or

(ii) a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains at least one and up to three atoms of N and, the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, said heteroaryl ring can be optionally substituted with one or more 1-pyrrolidinyl, 4- $[C_6 \text{ or } C_{10}]$ arylpiperazin-1-yl, 4- $[C_6 \text{ or } C_{10}]$ arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C1-C3)alkylenedioxy groups, or fused to a phenyl or pyridine ring, wherein the ring fusion is at a carbon-carbon double bond of the heteroaryl ring), or

(iii) a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or

(b)  $R^9$  is hydrogen or alkyl and  $R^{10}$  is  $Ar^*$ ; or

(c)  $R^9$  is hydrogen or alkyl,  $R^{10}$  is a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms are selected from the group consisting of oxygen, nitrogen and sulfur; or

(d)  $R^9$  and  $R^{10}$  are both alkyl groups; or

(e)  $R^9$  and  $R^{10}$  together with N form a heterocycle containing 4-10 ring atoms which can incorporate up to one additional heteroatom selected from the group of N, O or S in the ring, wherein the heterocycle is optionally substituted with (C<sub>6</sub>-or C<sub>10</sub>)aryl, (C<sub>6</sub>-or C<sub>10</sub>)arylalkyl, or a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings, each such heteroaryl can

be optionally substituted with one or more 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy; or

5 (f) R<sup>9</sup> and R<sup>10</sup> are both hydrogen; or

2. -NH<sub>2</sub>, and

e. X is a pharmaceutically acceptable anion, which may be absent if the compound provides a neutralizing salt,

(B) a pharmaceutically acceptable salt of the compound,

10 wherein aryl, Ar or Ar\* can be substituted with, in addition to any substitutions specifically noted, one or more general substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylamino, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, Ar\*C(O)-, Ar\*C(O)NH-, Ar\*O-, Ar\*-, Ar\*-alkyl-, carboxy, carboxyalkyl, 15 cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid (SO<sub>3</sub>H), 1-pyrrolidinyl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, and morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl; and

20 wherein heterocycles, except those of Ar or Ar\*, can be substituted with, in addition to any substitutions specifically noted, the following general substitutions: acylamino, alkanoyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, Ar\*C(O)-, Ar\*O-, Ar\*-, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, 25 mercapto, sulfamoyl, or trifluoromethyl.

2. The method of claim 1, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula -CH(R<sup>5</sup>)R<sup>6</sup>.

30 3. The method of claim 2, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula -CH(R<sup>5</sup>)-W-R<sup>7</sup>.

4. The method of claim 2, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula  $-\text{CH}(\text{R}^5)-\text{W}-\text{Rs}$ .

5. The method of claim 1, comprising administering an effective amount of a compound of formula I, wherein:

c. Ar can substituted on ring carbon atoms

1. with one or more substituents independently selected from the group

consisting hydrogen, acylamino, alkanoyl, alkanoylalkyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl,  $\omega$ -alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, halo, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid ( $-\text{SO}_3\text{H}$ ), alkylsulfonyl (alkyl $\text{SO}_2-$ ), alkylsulfinyl (alkyl $\text{SO}-$ ), alkylthio, trifluoromethyl, Ar\*, Ar\*-alkyl-, Ar\*-O-, Ar\* $\text{SO}_2-$ , Ar\* $\text{SO}-$ , Ar\*S-, Ar\* $\text{SO}_2\text{NH}-$ , Ar\*NH, (N-Ar\*)(N-alkyl)N-, Ar\*C(O)-, Ar\*C(O)NH-, Ar\*NH-C(O)-, and (N-Ar\*)(N-alkyl)N-C(O)-, wherein Ar\* may be substituted by one or more substituents as set forth above; or

2. two adjacent substitutions together with their ring carbons form a C<sub>6</sub>- or C<sub>10</sub>-aromatic fused ring system; or

3. two adjacent substitutions together with their ring carbons form a C<sub>5</sub>-C<sub>7</sub> fused cycloalkyl ring having no double bonds except the fused double bond of the Ar group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, amino, aminocarbonyl, carboxy, fluoro, or oxo, wherein multiple substituents are located on different carbon atoms of the cycloalkyl ring, except in the case of alkyl, and fluoro substituents, which can be located on the same or different carbon atoms;

d. Y is:

1. a group of the formula  $-\text{CH}(\text{R}^5)-\text{R}^6$

(a) R<sup>5</sup> is hydrogen or alkyl;

(b) wherein R<sup>6</sup> is

(1) hydrogen, alkyl, alkenyl, alkynyl, cyano, cyanoalkyl, or Rs,

wherein Rs is a [C<sub>6</sub> or C<sub>10</sub>]aryl or a heterocycle containing 4-10 ring atoms; or

- (2) a group of the formula  $-W-R^7$ , wherein  $R^7$  is alkyl, alkoxy, hydroxy, or  $Rs$ , wherein  $W$  is  $-C(=O)-$  or  $-S(O)_2-$ ;
- (3) a group of the formula  $-W-OR^8$  wherein  $R^8$  is hydrogen or alkyl,
- (4) a group of the formula  $-CH(OH)Rs$ ; or
- 5 (5) a group of the formula  $-W-N(R^9)R^{10}$ , wherein
- (a)  $R^9$  is hydrogen and  $R^{10}$  is an alkyl or cycloalkyl, optionally substituted by
- (i)  $[C_6 \text{ or } C_{10}]$ aryl, or
- (ii) a 5- or 6-membered heteroaryl ring that, in addition to
- 10 the general substitutions, can be optionally substituted with one or more halo or  $(C_1-C_3)$ alkylenedioxy groups, or fused to a phenyl ring, or
- (b)  $R^9$  is hydrogen or alkyl and  $R^{10}$  is  $Ar^*$ ; or
- (e)  $R^9$  and  $R^{10}$  together with  $N$  form a heterocycle containing 4-10
- 15 ring atoms which can incorporate up to one additional heteroatom selected from the group of  $N$ ,  $O$  or  $S$  in the ring, wherein the heterocycle is optionally substituted with  $(C_6\text{-or } C_{10})$ aryl,  $(C_6\text{-or } C_{10})$ arylalkyl, or a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of
- 20  $N$  for the 6-membered heteroaryl rings and from one to three atoms of  $N$  or one atom of  $O$  or  $S$  and zero to two atoms of  $N$  for the 5-membered heteroaryl rings, each such heteroaryl can be optionally substituted with one or more halo or  $(C_1-C_3)$ alkylenedioxy; or
- 25 (f)  $R^9$  and  $R^{10}$  are both hydrogen;
- or
2.  $-NH_2$ , and
- e.  $X$  is a pharmaceutically acceptable anion, which may be absent if the compound provides a neutralizing salt,
- 30 (B) a pharmaceutically acceptable salt of the compound,
- wherein aryl,  $Ar$  or  $Ar^*$  can be substituted with, in addition to any substitutions specifically noted, with one or more substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy,

alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, Ar<sup>\*</sup>C(O)-, Ar<sup>\*</sup>C(O)NH-, Ar<sup>\*</sup>O-, Ar<sup>\*</sup>-, Ar<sup>\*</sup>-alkyl-, carboxy, carboxyalkyl, cycloalkyl, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid (SO<sub>3</sub>H); and

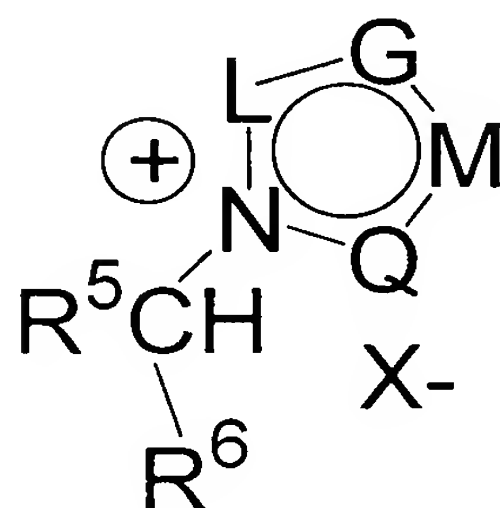
wherein heterocycles, except those of Ar or Ar<sup>\*</sup>, can be substituted with, in addition to any substitutions specifically noted, acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylsulfonyl, alkylsulfinyl, alkylthio, Ar<sup>\*</sup>C(O)-, Ar<sup>\*</sup>O-, Ar<sup>\*</sup>-, carboxy, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl, wherein multiple substituents are located on different atoms of the heterocyclic ring, with the proviso that alkyl, alkylcarbonyl, and fluoro substituents can be substituted on the same carbon atom of the heterocyclic ring.

6. The method of claim 5, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula -CH(R<sup>5</sup>)R<sup>6</sup>.

7. The method of claim 6, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula -CH(R<sup>5</sup>)-W-R<sup>7</sup>.

8. The method of claim 6, comprising administering an effective amount of a compound of formula I, wherein Y is according to formula -CH(R<sup>5</sup>)-W-R<sub>s</sub>.

9. The method of claim 1, wherein Y-Ar<sup>⊕</sup> • X<sup>-</sup> is



(II)

wherein G, L, M, and Q are independently O, S, N, N-R<sup>a</sup>, C, C-R<sup>b</sup>, C-R<sup>c</sup>, C-R<sup>d</sup>, wherein no more than one of G, L, M, or Q is O or S;



wherein

1.  $R^5$  is H;

2.  $R^6$  is

(1) cyano or

5 (2) a group of the formula  $-W-R^7$ , wherein  $R^7$  is alkyl or  $R_s$ , and W is -  
C(=O)- or -S(=O)-;

(3) a group of the formula  $-W-N(R^9)R^{10}$ , wherein

(a)  $R^9$  is hydrogen and  $R^{10}$  is an alkyl or cycloalkyl, optionally  
substituted by

10 (i)  $[C_6 \text{ or } C_{10}]$ aryl, or

(ii) a 5- or 6-membered heteroaryl ring, wherein the 6-membered  
heteroaryl ring contains at least one and up to three atoms of N  
and, the 5-membered heteroaryl ring contains from one to  
three atoms of N or one atom of O or S and zero to two atoms  
of N, said heteroaryl ring can be optionally substituted with  
one or more 1-pyrrolidinyl, 4- $[C_6 \text{ or } C_{10}]$ aryl piperazin-1-yl, 4-  
15  $[C_6 \text{ or } C_{10}]$ aryl piperidin-1-yl, azetidin-1-yl, and morpholin-4-  
yl, piperidin-1-yl, halo or  $(C_1-C_3)$ alkylenedioxy groups, or  
fused to a phenyl or pyridine ring, wherein the ring fusion is at  
20 a carbon-carbon double bond of the heteroaryl ring);

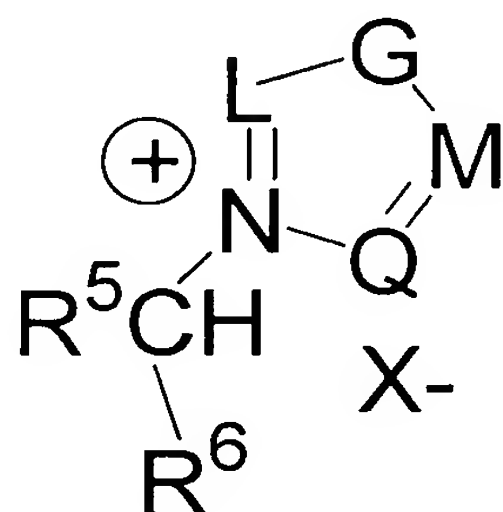
3.  $R^a$  is alkyl,  $Ar^*$ ,  $Ar^*$ alkyl, alkoxycarbonylalkylene-,  $Ar^*C(O)$ alkyl-,  
 $Ar^*$ sulfonylalkyl-, or  $Ar^*$ sulfinylalkyl-; and

4.  $R^b$ ,  $R^c$ , and  $R^d$  are

(a) independently selected from the group consisting hydrogen, acylamino,  
25 acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy,  
alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino,  $(C_1-$   
 $C_3)$ alkylenedioxy, alkylsulfonyl, alkylsulfinyl,  $\omega$ -alkylenesulfonic  
acid, alkylthio, allyl, amino,  $Ar^*C(O)-$ ,  $Ar^*O-$ ,  $Ar^*-$ ,  $Ar^*$ -alkyl-,  
carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo,  
30 trifluoromethyl, hydroxy,  $(C_2-C_6)$ hydroxyalkyl, mercapto, nitro,  
sulfamoyl, sulfonic acid ( $SO_3H$ ), 1-pyrrolidinyl-, 4- $[C_6 \text{ or } C_{10}]$ aryl  
piperazin-1-yl-, 4- $[C_6 \text{ or } C_{10}]$ aryl piperidin-1-yl, azetidin-1-yl,  
and morpholin-4-yl, piperidin-1-yl;



- (b) wherein any two of  $R^b$ ,  $R^c$ , and  $R^d$  are adjacent, together with their ring carbons form a  $C_6$  or  $C_{10}$  aromatic fused ring system;
- (c) wherein any two of  $R^b$ ,  $R^c$ , and  $R^d$  are adjacent, together with their ring carbons form a  $C_5$ - $C_7$  fused cycloalkyl ring having up to two double bonds including the fused double bond of the Ar group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo;
- (d) wherein any two of  $R^b$ ,  $R^c$ , and  $R^d$  are adjacent, together with their ring carbons form a fused five to eight membered heterocycle, , wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and  $S(O)_n$  wherein  $n=0,1$ , or  $2$ ; and
- (e) wherein any two of  $R^b$ ,  $R^c$ , and  $R^d$  are adjacent, together with their ring carbons form a fused five or six membered heteroaryl ring, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the fused heteroaryl ring consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and sulfur; and
10. The method of claim 9, wherein Ar is not tetrazole or pyrrole.
11. The method of claim 9, comprising administering an effective amount of a compound of formula II, wherein  $R^6$  is according to  $-CH(R^5)-W-R_s$
12. The method of claim 9, wherein aryl, Ar or  $Ar^*$  is substituted with, in addition to any substitutions specifically noted, one or more substituents selected from the group consisting of hydrogen, alkyl, amino, dialkylamino, 1-pyrrolidinyl, 4- $[C_6$  or  $C_{10}]$ arylpiperazin-1-yl, 4- $[C_6$  or  $C_{10}]$ arylpiperidin-1-yl, azetidin-1-yl, and morpholin-4-yl, piperidin-1-yl.
13. The method of claim 9, wherein  $Y-Ar^{\oplus} \bullet X^-$  is



(III)

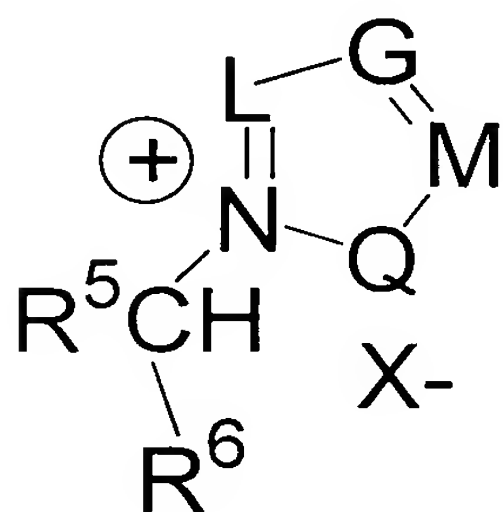
wherein G is O, S, or N-R<sup>a</sup>;

M is N or C-R<sup>b</sup>;

Q is N or C-R<sup>c</sup>; and

5 L is N or C-R<sup>d</sup>.

14. The method of claim 9, wherein Y-Ar<sup>⊕</sup> • X<sup>-</sup> is



(IV)

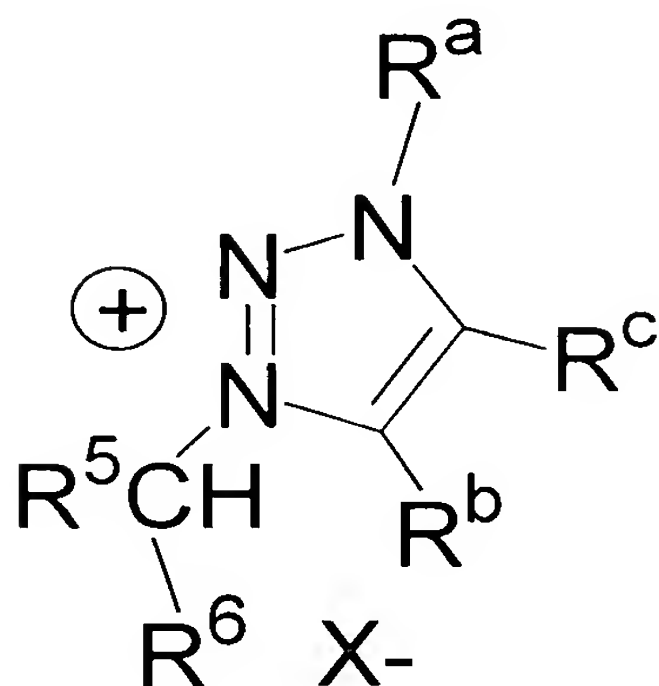
10 wherein G is N or C-R<sup>c</sup>;

M is N or C-R<sup>b</sup>;

Q is O, S, or N-R<sup>a</sup>; and

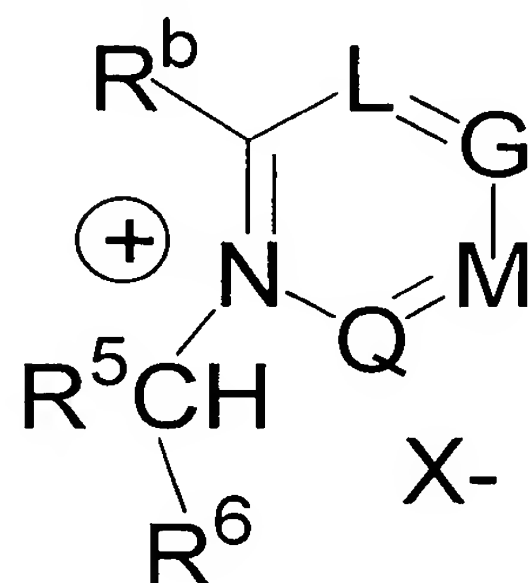
L is N or C-R<sup>d</sup>.

15 15. The method of claim 9, wherein Y-Ar<sup>⊕</sup> • X<sup>-</sup> is



(IV)

16. The method of claim 1, wherein  $Y-Ar^{\oplus} \bullet X^{-}$  is



(V)

wherein L, G, M, Q, or R are independently N, C-R<sup>c</sup>, C-R<sup>d</sup>, C-R<sup>e</sup>, C-R<sup>f</sup>;

5 wherein

1. R<sup>5</sup> is H;

2. R<sup>6</sup> is

(1) cyano or

(2) a group of the formula -W-R<sup>7</sup>, wherein R<sup>7</sup> is alkyl or Rs, and W is -  
 10 C(=O)- or -S(=O)-;

3. R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, and R<sup>e</sup> are

(a) independently selected from the group consisting hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy,

alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C<sub>1</sub>-

15 C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, Ar<sup>\*</sup>C(O)-, Ar<sup>\*</sup>O-, Ar<sup>\*</sup>-, Ar<sup>\*</sup>-alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo,

trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro,

sulfamoyl, sulfonic acid (SO<sub>3</sub>H), 1-pyrrolidinyl-, 4-[C<sub>6</sub> or

20 C<sub>10</sub>]arylpiperazin-1-yl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, and morpholin-4-yl, piperidin-1-yl;

(b) where any two of R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, and R<sup>e</sup> are adjacent, together with their ring carbons form a C<sub>6</sub>- or C<sub>10</sub>- aromatic fused ring system;

(c) where any two of R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, and R<sup>e</sup> are adjacent, together with their ring carbons form a C<sub>5</sub>-C<sub>7</sub> fused cycloalkyl ring having up to two double bonds including the fused double bond of the Ar group, which cycloalkyl ring can be substituted by one or more of the group

25

consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo;

5 (d) wherein any two of  $R^b$ ,  $R^c$ ,  $R^d$ , and  $R^e$  are adjacent, together with their ring carbons form a fused five to eight membered heterocycle, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and  $S(O)_n$  wherein  $n=0,1$ , or 2;

10 (e) wherein any two of  $R^b$ ,  $R^c$ ,  $R^d$ , and  $R^e$  are adjacent, together with their ring carbons form a fused five or six membered heteroaryl ring, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the fused heteroaryl ring consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and sulfur, and wherein Ar has no more than three nitrogen atoms in the ring.

15 17. The method of claim 1, wherein Ar is substituted on a said ring nitrogen with amino.

20 18. The method of claim 17, wherein Ar is further substituted with up to two aminos.

19. The method of claim 1, wherein:

25 a. Ar is a five or six membered heteroaryl ring having a first ring nitrogen and optionally second or third ring nitrogens, with the remaining ring atoms being carbon, oxygen, or sulfur, provided the first nitrogen of Ar is a quaternary nitrogen and Ar is not thiazolium, oxazolium or imidazolium;

b. Y is substituted on the first ring nitrogen, with the proviso that if Ar is pyrazole, indazole, (1,2,3)-triazole, benzotriazole, or (1,2,4)-triazole, the second ring nitrogen is substituted with

30 1. alkyl or alkoxycarbonylalkylene;

2.  $Ar^*$  ; or

3.  $Ar^*$ alkyl-,  $Ar^*C(O)$ alkyl-,  $Ar^*$ sulfonylalkyl-, or  $Ar^*$ sulfinylalkyl-; and

c. Ar can be substituted on ring carbon atoms

1. with one or more substituents independently selected from the group consisting  $\omega$ -alkylenesulfonic acid, carbamoyl, Ar\*, Ar\*-alkyl-, Ar\*-O-, Ar\*SO<sub>2</sub>-, Ar\*SO-, Ar\*S-, Ar\*SO<sub>2</sub>NH-, Ar\*NH, (N-Ar\*)(N-alkyl)N-, Ar\*C(O)-, Ar\*C(O)NH-, Ar\*NH-C(O)-, and (N-Ar\*)(N-alkyl)N-C(O)-;  
 5 or
2. two adjacent substitutions together with their ring carbons form a C<sub>6</sub>- or C<sub>10</sub>-aromatic fused ring system; or
3. two adjacent substitutions together with their ring carbons form a C<sub>5</sub>-C<sub>7</sub> fused cycloalkyl ring having up to two double bonds including the fused double  
 10 bond of the Ar group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, aminocarbonyl, carboxy, fluoro, or oxo; or
4. two adjacent substitutions together with their ring carbons form a fused five to  
 15 eight membered heterocycle, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and S(O)<sub>n</sub>, wherein n=0,1, or 2; or
5. two adjacent substitutions together with their ring carbons form a fused five or  
 20 six membered heteroaryl ring, wherein the ring fusion is at a carbon-carbon double bond of Ar, wherein the fused heteroaryl ring consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, and sulfur;

d. Y is:

1. a group of the formula -CH(R<sup>5</sup>)-R<sup>6</sup>  
 25 (a) R<sup>5</sup> is hydrogen, alkyl-, cycloalkyl-, alkenyl-, alkynyl-, hydroxy[C<sub>1</sub> to C<sub>6</sub>]alkyl, [C<sub>6</sub> or C<sub>10</sub>]aryl, or independently the same as R<sup>6</sup>;  
 (b) wherein R<sup>6</sup> is  
 (1) hydrogen, alkyl (which may be substituted by alkoxycarbonyl)-, alkenyl, alkynyl, cyano-, cyanoalkyl-, or Rs, wherein Rs is a [C<sub>6</sub>  
 30 or C<sub>10</sub>]aryl or a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or

- (2) a group of the formula  $-W-R^7$ , wherein  $R^7$  is alkyl, alkoxy, hydroxy, or  $Rs$ , wherein  $W$  is  $-C(=O)-$  or  $-S(O)_2-$ ;
- (3) a group of the formula  $-W-OR^8$  wherein  $R^8$  is hydrogen or alkyl,
- (4) a group of the formula  $-CH(OH)Rs$ ; or
- 5 (5) a group of the formula  $-W-N(R^9)R^{10}$ , wherein
- (a)  $R^9$  is hydrogen and  $R^{10}$  is an alkyl or cycloalkyl, optionally substituted by
- (i)  $[C_6 \text{ or } C_{10}]$ aryl, or
- 10 (ii) a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains at least one and up to three atoms of N and, the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, said heteroaryl ring can be optionally substituted with one or more
- 15 halo or (C1-C3)alkylenedioxy groups, or fused to a phenyl, or
- (iii) a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or
- 20 (b)  $R^9$  is hydrogen or alkyl and  $R^{10}$  is  $Ar^*$ ; or
- (c)  $R^9$  is hydrogen or alkyl,  $R^{10}$  is a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms are selected from the group consisting of oxygen, nitrogen and sulfur; or
- (d)  $R^9$  and  $R^{10}$  are both alkyl groups; or
- 25 (e)  $R^9$  and  $R^{10}$  together with N form a heterocycle containing 4-10 ring atoms which can incorporate up to one additional heteroatom selected from the group of N, O or S in the ring, wherein the heterocycle is optionally substituted with  $(C_6\text{-or } C_{10})$ aryl,  $(C_6\text{-or } C_{10})$ arylalkyl, or a 5- or 6-membered
- 30 heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings, each such heteroaryl can

be optionally substituted with one or more halo or (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy; or

(f) R<sup>9</sup> and R<sup>10</sup> are both hydrogen; or

2. -NH<sub>2</sub>, and

- 5 e. X is a pharmaceutically acceptable anion, which may be absent if the compound provides a neutralizing salt,

(B) a pharmaceutically acceptable salt of the compound,

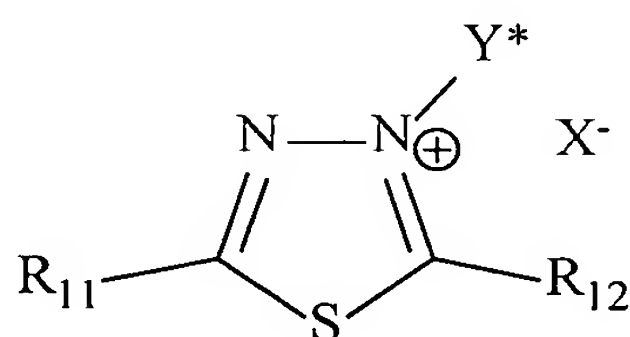
wherein aryl, Ar or Ar\* can be substituted with, in addition to any substitutions

specifically noted, one or more substituents selected from the group consisting of

10 acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, Ar\*C(O)-, Ar\*C(O)NH-, Ar\*O-, Ar\*-, Ar\*-alkyl-, carboxy, carboxyalkyl, cycloalkyl, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, 15 sulfonic acid (SO<sub>3</sub>H); and

wherein heterocycles, except those of Ar or Ar\*, can be substituted with, in addition to any substitutions specifically noted, acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylsulfonyl, alkylsulfinyl, alkylthio, Ar\*C(O)-, Ar\*O-, Ar\*-, carboxy, fluoro, fluoroalkyl, difluoroalkyl, 20 hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

20. A compound of formula VI:



(VI)

wherein

- 25 a. one of R<sup>11</sup> and R<sup>12</sup> is hydrogen, and the other is selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, allyl, amino, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl,



sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl, Ar<sup>2</sup> (wherein Ar<sup>2</sup> is C<sub>6</sub> or C<sub>10</sub> aryl), Ar<sup>2</sup>-alkyl, Ar<sup>2</sup>-O, Ar<sup>2</sup>SO<sub>2</sub>-, Ar<sup>2</sup>SO-, Ar<sup>2</sup>S-, Ar<sup>2</sup>SO<sub>2</sub>NH-, Ar<sup>2</sup>NH, (N-Ar<sup>2</sup>)(N-alkyl)N-,

5 Ar<sup>2</sup>C(O)-, Ar<sup>2</sup>C(O)NH-, Ar<sup>2</sup>NH-C(O)-, or (N-Ar<sup>2</sup>)(N-alkyl)N-C(O)-;

b. Y<sup>\*</sup> is a group of the formula -CH(R<sup>5</sup>)-R<sup>6</sup> wherein

(a) R<sup>5</sup> is hydrogen, alkyl-, cycloalkyl-, alkenyl-, alkynyl-, aminoalkyl-,

dialkylaminoalkyl-, (N-[C<sub>6</sub> or C<sub>10</sub>]aryl)(N-alkyl)aminoalkyl-, piperidin-1-

ylalkyl-, 1-pyrrolidinylalkyl, azetidinyllalkyl, 4-alkylpiperazin-1-ylalkyl, 4-

10 alkylpiperidin-1-ylalkyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-ylalkyl, 4-[C<sub>6</sub> or

C<sub>10</sub>]arylpiperidin-1-ylalkyl, azetidin-1-ylalkyl, morpholin-4-ylalkyl,

thiomorpholin-4-ylalkyl, piperidin-1-ylalkyl, [C<sub>6</sub> or C<sub>10</sub>]aryl, or

independently the same as R<sup>6</sup>;

(b) R<sup>6</sup> is

15 (1) cyano or Rs, wherein Rs is a [C<sub>6</sub> or C<sub>10</sub>]aryl or a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur;

(2) a group of the formula -W-Rs, wherein W is -C(=O)- or -S(O)<sub>n</sub>- where n=1 or 2;

20 (3) a group of the formula -W-N(R<sup>9</sup>)R<sup>10</sup>, wherein

[a] R<sup>9</sup> is hydrogen and R<sup>10</sup> is an alkyl or cycloalkyl, optionally substituted by

(i) [C<sub>6</sub> or C<sub>10</sub>]aryl, or

(ii) a 5- or 6-membered heteroaryl ring, wherein the 6-membered

25 heteroaryl ring contains one to three atoms of N, and the 5-

membered heteroaryl ring contains from one to three atoms of N

or one atom of O or S and zero to two atoms of N, said heteroaryl

ring can be optionally substituted with one or more 1-pyrrolidinyl,

4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl,

30 azetidin-1-yl, and morpholin-4-yl, thiomorpholin-4-yl, piperidin-

1-yl, halo or (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy groups, or fused to a

substituted phenyl or pyridine ring, wherein the ring fusion is at a

carbon-carbon double bond of the heteroaryl ring, or

(iii) a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or

[b]  $R^9$  is hydrogen or lower alkyl and  $R^{10}$  is  $Ar^2$ ; or

5 [c]  $R^9$  is hydrogen or lower alkyl, and  $R^{10}$  is a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms are selected from the group consisting of oxygen, nitrogen and sulfur, said heterocycle; or

[d]  $R^9$  and  $R^{10}$  are both alkyl groups; or

10 [e]  $R^9$  and  $R^{10}$  together with N form a heterocycle containing 4-10 ring atoms which can incorporate up to one additional heteroatom selected from the group of N, O or S in the ring, wherein the heterocycle is optionally substituted with (C<sub>6</sub>-or C<sub>10</sub>)aryl, (C<sub>6</sub>-or C<sub>10</sub>)arylalkyl, or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each such heteroaryl can be optionally substituted with one or more 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy; or

15

20

[f]  $R^9$  and  $R^{10}$  are both hydrogen; and

c. X is a pharmaceutically acceptable anion, or

(B) a pharmaceutically acceptable salt of the compound,

wherein aryl or  $Ar^*$  can be substituted with, in addition to any substitutions specifically

25 noted, one or more general substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl,  $\omega$ -alkylenesulfonic acid, alkylthio, allyl, amino,  $Ar^2C(O)-$ ,  $Ar^2C(O)NH-$ ,  $Ar^2O-$ ,  $Ar^2-$ ,  $Ar^2$ -alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl;

30

wherein heterocycles, except those of  $\text{Ar}^2$ , can be substituted with, in addition to any substitutions specifically noted, the following general substitutions: acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino,  $\text{Ar}^2\text{C}(\text{O})-$ ,  $\text{Ar}^2\text{O}-$ ,  $\text{Ar}^2-$ , carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl;

wherein the compound of formula VI differs from a salt of 3-[2-(4-bromophenyl)-2-oxoethyl]-1,3,4-thiadiazolium by one or more of the lack or replacement of the 4-bromo substitution, or the presence of one or more additional substitutions; and

wherein the compound of formula VI differs from a salt of 3-(phenylmethyl)-1,3,4-thiadiazolium by the presence of one or more additional substitutions.

21. The compound of claim 20, wherein  $\text{Y}^*$  is according to formula  $-\text{CH}(\text{R}^5)-\text{W}-\text{Rs}$ .

15 <sup>22</sup>~~25~~ The compound of Claim 20, wherein

a.  $\text{R}^{11}$  and  $\text{R}^{12}$  are independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl,  $(\text{C}_1-\text{C}_3)$ alkylenedioxy, allyl,  $\omega$ -alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, halo, hydroxy,  $(\text{C}_2-\text{C}_6)$ hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl,  $\text{Ar}^2$ ,  $\text{Ar}^2$ -alkyl,  $\text{Ar}^2\text{-O}$ ,  $\text{Ar}^2\text{SO}_2-$ ,  $\text{Ar}^2\text{SO}-$ ,  $\text{Ar}^2\text{S}-$ ,  $\text{Ar}^2\text{SO}_2\text{NH}-$ ,  $\text{Ar}^2\text{NH}$ ,  $(\text{N}-\text{Ar}^2)(\text{N-alkyl})\text{N}-$ ,  $\text{Ar}^2\text{C}(\text{O})-$ ,  $\text{Ar}^2\text{C}(\text{O})\text{NH}-$ ,  $\text{Ar}^2\text{NH-C}(\text{O})-$ , and  $(\text{N}-\text{Ar}^2)(\text{N-alkyl})\text{N-C}(\text{O})-$ ; or

b. Y is a group of the formula  $-\text{CH}(\text{R}^5)-\text{R}^6$  wherein

25 (a)  $\text{R}^5$  is hydrogen or alkyl;

(b)  $\text{R}^6$  is

(1) cyano or  $\text{Rs}$ ;

(2) a group of the formula  $-\text{W}-\text{Rs}$ , wherein W is  $-\text{C}(=\text{O})-$  or  $-\text{S}(\text{O})_n-$  where  $n=1$  or 2;

30 (3) a group of the formula  $-\text{W}-\text{N}(\text{R}^9)\text{R}^{10}$ , wherein

[a]  $\text{R}^9$  is hydrogen and  $\text{R}^{10}$  is an alkyl or cycloalkyl, optionally substituted by

(i)  $[\text{C}_6$  or  $\text{C}_{10}]$ aryl, or

methods  
 II formula VI same  
 III formula VII six  
 IV from III pyrimidin

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- (ii) a 5- or 6-membered heteroaryl ring, wherein the optional substitutions on the heteroaryl ring are, in addition to the general substitutions, one or more halo or (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy groups, or form a fused a substituted phenyl, or
- 5 (iii) a heterocycle containing 4-10 ring atoms; or
- [b] R<sup>9</sup> is hydrogen or lower alkyl and R<sup>10</sup> is Ar<sup>2</sup>; or
- [c] R<sup>9</sup> is hydrogen or lower alkyl, and R<sup>10</sup> is a heterocycle containing 4-10 ring atoms; or
- [d] R<sup>9</sup> and R<sup>10</sup> are both alkyl groups; or
- 10 [e] R<sup>9</sup> and R<sup>10</sup> together with N form a heterocycle containing 4-10 ring atoms, wherein each heteroaryl thereon can, in addition to the general substitutions, be optionally substituted with one or more halo or (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy; or
- [f] R<sup>9</sup> and R<sup>10</sup> are both hydrogen; and
- 15 g. X is a pharmaceutically acceptable anion, or
- (B) a pharmaceutically acceptable salt of the compound, wherein aryl or Ar<sup>2</sup> can be substituted with, in addition to any substitutions specifically noted, one or more general substituents selected from the group consisting of
- 20 acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, Ar<sup>2</sup>C(O)-, Ar<sup>2</sup>C(O)NH-, Ar<sup>2</sup>O-, Ar<sup>2</sup>-, Ar<sup>2</sup>-alkyl-, carboxy, carboxyalkyl, cycloalkyl, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid; and
- wherein heterocycles, except those of Ar<sup>2</sup>, can be substituted with, in addition to any
- 25 substitutions specifically noted, the following general substitutions: acylamino, alkanoyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylsulfonyl, alkylsulfinyl, alkylthio, Ar<sup>2</sup>C(O)-, Ar<sup>2</sup>O-, Ar<sup>2</sup>-, carboxy, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

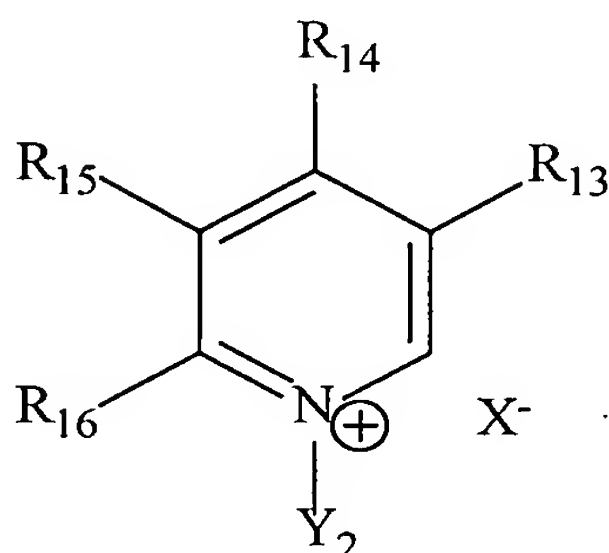
- 23  
30 ~~24~~  
^ The compound of claim 23, wherein Y\* is according to formula -CH(R<sup>5</sup>)-W-Rs.
- 24  
~~25~~  
^ A compound of claim 20 selected from:
- 5-Amino-3-carbamoylmethyl-[1,3,4]-thiadiazolium bromide;

2-Amino-3-(4-chloro-benzyl)-[1,3,4]-thiadiazolium chloride; and  
2-Amino-3-(4-fluoro-benzyl)-[1,3,4]-thiadiazolium bromide.

- 25  
26. <sup>^</sup> A pharmaceutical composition comprising:  
5 a compound of one of claims 20 to 25; and  
a pharmaceutically acceptable excipient.

- 26  
27. A method of treating an indication of the invention with a pharmaceutically  
effective amount of a compound of one of claims 20 to 25.

- 10 27  
28. <sup>^</sup> A compound of formula VI:



(VII)

wherein

a.  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$

- 15 1. are independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl,  
alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl,  
alkylamino, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, allyl, amino, ω-alkylenesulfonic acid,  
carbamoyl, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, hydroxy, (C<sub>2</sub>-  
C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl,  
20 alkylsulfinyl, alkylthio, trifluoromethyl, azetidin-1-yl, morpholin-4-yl,  
thiomorpholin-4-yl, piperidin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, 4-[C<sub>6</sub> or  
C<sub>10</sub>]arylpiperazin-1-yl, Ar<sup>3</sup> (wherein Ar<sup>3</sup> is C<sub>6</sub> or C<sub>10</sub> aryl), Ar<sup>3</sup>-alkyl, Ar<sup>3</sup>-O,  
Ar<sup>3</sup>SO<sub>2</sub>-, Ar<sup>3</sup>SO-, Ar<sup>3</sup>S-, Ar<sup>3</sup>SO<sub>2</sub>NH-, Ar<sup>3</sup>NH-, (N-Ar<sup>3</sup>)(N-alkyl)N-, Ar<sup>3</sup>C(O)-,  
Ar<sup>3</sup>C(O)NH-, Ar<sup>3</sup>NH-C(O)-, and (N-Ar<sup>3</sup>)(N-alkyl)N-C(O)-, or together R<sub>1</sub> and R<sub>2</sub>  
25 comprise methylenedioxy; or  
2. form, with an adjacent pair from  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$ , together with their ring  
carbons, a C<sub>6</sub>- or C<sub>10</sub>- aromatic fused ring system; or

3. form, with an adjacent pair from  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$ , together with their ring carbons, a  $C_5$ - $C_7$  fused cycloalkyl ring having up to two double bonds including the fused double bond of the pyridinium containing ring, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxy carbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo substituents; or
4. form, with an adjacent pair from  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$ , together with their ring carbons, a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring may be optionally substituted with one or more 1-pyrrolidinyl-, 4- $[C_6$  or  $C_{10}]$ arylpiperazin-1-yl, 4- $[C_6$  or  $C_{10}]$ arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or  $(C_1$ - $C_3)$ alkylenedioxy groups; or
5. form, with an adjacent pair from  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$ , together with their ring carbons, a five to eight membered heterocycle, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, and  $S(O)_n$ , where  $n=0,1$ , or 2;
- b.  $Y^2$  is a group of the formula  $-CH(R^5)-R^6$  wherein
- (a)  $R^5$  is hydrogen, alkyl-, cycloalkyl-, alkenyl-, alkynyl-, aminoalkyl-, dialkylaminoalkyl-, (N- $[C_6$  or  $C_{10}]$ aryl)(N-alkyl)aminoalkyl-, piperidin-1-ylalkyl-, 4-pyrrolidin-1-ylalkyl, azetidylalkyl, 4-alkylpiperazin-1-ylalkyl, 4-alkylpiperidin-1-ylalkyl, 4- $[C_6$  or  $C_{10}]$ arylpiperazin-1-ylalkyl, 4- $[C_6$  or  $C_{10}]$ arylpiperidin-1-ylalkyl, azetidin-1-ylalkyl, morpholin-4-ylalkyl, thiomorpholin-4-ylalkyl, piperidin-1-ylalkyl,  $[C_6$  or  $C_{10}]$ aryl, or independently the same as  $R^6$ ;
- (b)  $R^6$  is phenyl substituted at the para position with chloro or fluoro;
- (2) a group of the formula  $-W-R_s$ , wherein W is  $-C(=O)-$  or  $-S(O)_n-$  where  $n=1$  or 2;
- (3) a group of the formula  $-W-N(R^9)R^{10}$ , wherein
- [a]  $R^9$  is hydrogen and  $R^{10}$  is an alkyl or cycloalkyl, optionally substituted by
- (i)  $[C_6$  or  $C_{10}]$ aryl, or



- 5 (ii) a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, said heteroaryl ring can be optionally substituted with one or more 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, and morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy groups, or fused to a phenyl or pyridine ring, wherein the ring fusion is at a carbon-carbon double bond of the heteroaryl ring, or
- 10 (iii) a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; or
- [b] R<sup>9</sup> is hydrogen or lower alkyl and R<sup>10</sup> is Ar<sup>3</sup>; or
- 15 [c] R<sup>9</sup> is hydrogen or lower alkyl, and R<sup>10</sup> is a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms are selected from the group consisting of oxygen, nitrogen and sulfur, said heterocycle; or
- [d] R<sup>9</sup> and R<sup>10</sup> are both alkyl groups; or
- 20 [e] R<sup>9</sup> and R<sup>10</sup> together with N form a heterocycle containing 4-10 ring atoms which can incorporate up to one additional heteroatom selected from the group of N, O or S in the ring, wherein the heterocycle is optionally substituted with (C<sub>6</sub>-or C<sub>10</sub>)aryl, (C<sub>6</sub>-or C<sub>10</sub>)arylalkyl, or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each such heteroaryl can be optionally substituted with one or more 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C<sub>1</sub>-
- 25 C<sub>3</sub>)alkylenedioxy; or
- 30 [f] R<sup>9</sup> and R<sup>10</sup> are both hydrogen;

c. X is a pharmaceutically acceptable anion, or

(B) a pharmaceutically acceptable salt of the compound,



wherein aryl or Ar<sup>3</sup> can be substituted with, in addition to any substitutions specifically noted, one or more general substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, Ar<sup>3</sup>C(O)-, Ar<sup>3</sup>C(O)NH-, Ar<sup>3</sup>O-, Ar<sup>3</sup>-, Ar<sup>3</sup>-alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl;

wherein heterocycles, except those of Ar<sup>3</sup>, can be substituted with, in addition to any substitutions specifically noted, the following general substitutions: acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, Ar<sup>3</sup>C(O)-, Ar<sup>3</sup>O-, Ar<sup>3</sup>-, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl;

wherein, if the compound of formula VII has a core structure comprising a pyridinium ring having a 2-aryl-2-oxoethyl substitution at the 1 position, wherein the aryl can be substituted, and a formyl which may be substituted at the 3 position, one or both of the following applies:

the compound of formula VII differs from a salt of pyridinium compound having a 1-(2-aryl-2-oxoethyl), wherein the aryl can be substituted, and a formyl which may be substituted at the 3 position by at least one additional substitution at R<sup>14</sup>, R<sup>15</sup> or R<sup>16</sup>, or the aryl of 2-aryl-2-oxoethyl is phenyl and is substituted at the para position with an electron withdrawing group selected from fluoro, chloro, nitro, trifluoromethyl, and carbamoyl; and

wherein the compound of formula VII differs from a salt of 1-[2-(4-methylphenyl)-2-oxoethyl]-pyridinium by one or more of the lack or replacement of the methyl substitution, or the presence of one or more additional substitutions.

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The compound of claim 28, wherein Y<sup>2</sup> is according to formula -CH(R<sup>5</sup>)-W-Rs.

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The compound of Claim 28, wherein an adjacent pair from  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$ , together with their ring carbons, form a  $C_6$ - or  $C_{10}$ - aromatic fused ring which can be substituted by one or more halo, amino, alkyl, sulfonic acid, alkylsulfonyl or  $\omega$ -alkylenesulfonic acid groups, or a  $C_1$ - $C_3$  alkylenedioxy group.

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The compound of claim 28, wherein

a.  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$

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1. are independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, ( $C_1$ - $C_3$ )alkylenedioxy, allyl,  $\omega$ -alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, halo, hydroxy, ( $C_2$ - $C_6$ )hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl,  $Ar^3$ ,  $Ar^3$ -alkyl,  $Ar^3$ -O,  $Ar^3SO_2$ -,  $Ar^3SO$ -,  $Ar^3S$ -,  $Ar^3SO_2NH$ -,  $Ar^3NH$ -, (N- $Ar^3$ )(N-alkyl)N-,  $Ar^3C(O)$ -,  $Ar^3C(O)NH$ -,  $ArNH-C(O)$ -, and (N- $Ar$ )(N-alkyl)N-C(O)-; or

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2. form, with an adjacent pair from  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$ , together with their ring carbons, a  $C_6$ - or  $C_{10}$ - aromatic fused ring system; or

3. form, with an adjacent pair from  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$ , together with their ring carbons, a  $C_5$ - $C_7$  fused cycloalkyl, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxy carbonyl, aminocarbonyl, carboxy, fluoro, or oxo substituents; or

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4. form, with an adjacent pair from  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$ , together with their ring carbons, a 5- or 6-membered heteroaryl ring, wherein each heteroaryl ring may, in addition to the general substitutions, be optionally substituted with one or more halo or ( $C_1$ - $C_3$ )alkylenedioxy groups; or

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5. form, with an adjacent pair from  $R^{13}$ ,  $R^{14}$ ,  $R^{15}$  and  $R^{16}$ , together with their ring carbons, a five to eight membered heterocycle;

b. Y is a group of the formula  $-CH(R^5)-R^6$  wherein

(a)  $R^5$  is hydrogen or alkyl;

(b)  $R^6$  is

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(1) cyano or  $Rs$ ;

(2) a group of the formula  $-W-Rs$ , wherein W is  $-C(=O)-$  or  $-S(O)_n-$  where  $n=1$  or 2;

(3) a group of the formula  $-W-N(R^9)R^{10}$ , wherein

[a]  $R^9$  is hydrogen and  $R^{10}$  is an alkyl or cycloalkyl, optionally substituted by

(i)  $[C_6 \text{ or } C_{10}]$ aryl, or

5 (ii) a 5- or 6-membered heteroaryl ring, wherein said heteroaryl ring can, in addition to the general substitutions, be optionally substituted with one or more halo or  $(C_1-C_3)$ alkylenedioxy groups, or fused to a substituted phenyl, or

(iii) a heterocycle containing 4-10 ring atoms; or

10 [b]  $R^9$  is hydrogen or lower alkyl and  $R^{10}$  is  $Ar^3$ ; or

[c]  $R^9$  is hydrogen or lower alkyl, and  $R^{10}$  is a heterocycle; or

[d]  $R^9$  and  $R^{10}$  are both alkyl groups; or

[e]  $R^9$  and  $R^{10}$  together with N form a heterocycle, wherein each

heteroaryl thereon can, in addition to the general substitutions, be

15 optionally substituted with one or more halo or  $(C_1-C_3)$ alkylenedioxy;

or

[f]  $R^9$  and  $R^{10}$  are both hydrogen; and

g. X is a pharmaceutically acceptable anion, or

(B) a pharmaceutically acceptable salt of the compound,

20 wherein aryl or  $Ar^3$  can be substituted with, in addition to any substitutions specifically noted, one or more general substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl,  $(C_1-C_3)$ alkylenedioxy, alkylsulfonyl, alkylsulfinyl,  $\omega$ -alkylenesulfonic acid, alkylthio, allyl,  $Ar^3C(O)-$ ,  $Ar^3C(O)NH-$ ,  
 25  $Ar^3O-$ ,  $Ar^3-$ ,  $Ar^3$ -alkyl-, carboxy, carboxyalkyl, cycloalkyl, halo, trifluoromethyl, hydroxy,  $(C_2-C_6)$ hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid; and wherein heterocycles, except those of Ar, can be substituted with, in addition to any substitutions specifically noted, the following general substitutions: acylamino, alkanoyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylsulfonyl, alkylsulfinyl, alkylthio,  $Ar^3C(O)-$ ,  $Ar^3O-$ ,  $Ar^3-$ , carboxy, fluoro, fluoroalkyl,  
 30 difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

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The compound of claim 31, wherein  $Y^2$  is according to formula  $-CH(R^5)-W-R_s$ .

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A compound of claim 28, selected from:

3-(aminocarbonyl)-1-[2-(4-chlorophenyl)-2-oxoethyl]pyridinium chloride;

3-(aminocarbonyl)-1-benzylpyridinium bromide;

5 3-Carbamoyl-1-(4-methoxy-benzyl)-pyridinium chloride; and

3-Carbamoyl-1-[2-(4-fluoro-phenyl)-2-oxo-ethyl]-pyridinium chloride.

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A pharmaceutical composition comprising:

a compound of one of claims 28 to 33; and

10 a pharmaceutically acceptable excipient.

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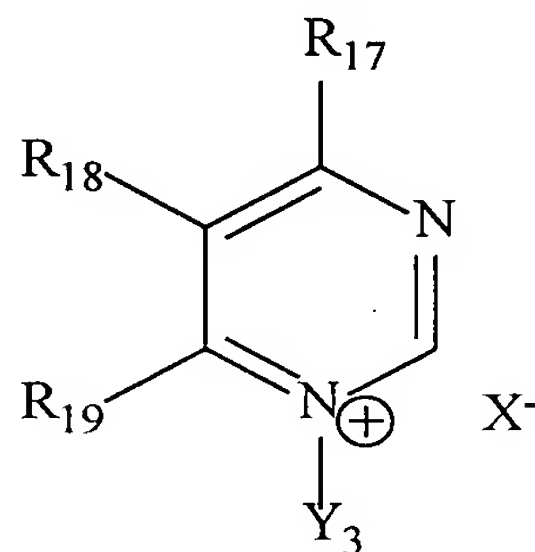
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A method of treating an indication of the invention with a pharmaceutically effective amount of a compound of one of claims 28 to 33.

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A compound of formula VIII:



(VIII)

wherein

a.  $R^{17}$ ,  $R^{18}$  and  $R^{19}$ 

1. are independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino,  $(C_1-C_3)$ alkylenedioxy, allyl; amino,  $\omega$ -alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, hydroxy,  $(C_2-C_6)$ hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, 4- $[C_6$  or  $C_{10}]$ arylpiperidin-1-yl, 4- $[C_6$  or  $C_{10}]$ arylpiperazin-1-yl,  $Ar^4$  (wherein  $Ar^2$  is  $C_6$  or  $C_{10}$  aryl),  $Ar^4$ -alkyl,  $Ar^4$ -O,  $Ar^4SO_2$ -,  $Ar^4SO$ -,  $Ar^4S$ -,  $Ar^4SO_2NH$ -,  $Ar^4NH$ ,  $(N-Ar^4)(N-alkyl)N$ -,  $Ar^4C(O)$ -,

$\text{Ar}^4\text{C}(\text{O})\text{NH}-$ ,  $\text{Ar}^4\text{NH}-\text{C}(\text{O})-$ , and  $(\text{N}-\text{Ar}^4)(\text{N-alkyl})\text{N}-\text{C}(\text{O})-$ , or together  $\text{R}_1$  and  $\text{R}_2$  comprise methylenedioxy; or

2. form, with an adjacent pair from  $\text{R}^{17}$ ,  $\text{R}^{18}$  and  $\text{R}^{19}$ , together with their ring carbons, a  $\text{C}_6$ - or  $\text{C}_{10}$ - aromatic fused ring system; or
- 5 3. form, with an adjacent pair from  $\text{R}^{17}$ ,  $\text{R}^{18}$  and  $\text{R}^{19}$ , together with their ring carbons, a  $\text{C}_5$ - $\text{C}_7$  fused cycloalkyl ring having up to two double bonds including the fused double bond of the pyridinium containing ring, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo substituents; or
- 10 4. form, with an adjacent pair from  $\text{R}^{17}$ ,  $\text{R}^{18}$  and  $\text{R}^{19}$ , together with their ring carbons, a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring may be optionally substituted with one or more 1-  
 15 pyrrolidinyl-, 4- $[\text{C}_6$  or  $\text{C}_{10}]$ arylpiperazin-1-yl, 4- $[\text{C}_6$  or  $\text{C}_{10}]$ arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or  $(\text{C}_1$ - $\text{C}_3$ )alkylenedioxy groups; or
- 20 5. form, with an adjacent pair from  $\text{R}^{17}$ ,  $\text{R}^{18}$  and  $\text{R}^{19}$ , together with their ring carbons, a five to eight membered heterocycle, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, and  $\text{S}(\text{O})_n$ , where  $n=0,1$ , or 2;
- b.  $\text{Y}^3$  is a group of the formula  $-\text{CH}(\text{R}^5)-\text{R}^6$  wherein
  - (a)  $\text{R}^5$  is hydrogen, alkyl-, cycloalkyl-, alkenyl-, alkynyl-, aminoalkyl-, dialkylaminoalkyl-,  $(\text{N}-[\text{C}_6$  or  $\text{C}_{10}]$ aryl)(N-alkyl)aminoalkyl-, piperidin-1-ylalkyl-, 1-pyrrolidin-1-ylalkyl, azetidinyllalkyl, 4-alkylpiperazin-1-ylalkyl, 4-alkylpiperidin-1-ylalkyl, 4- $[\text{C}_6$  or  $\text{C}_{10}]$ arylpiperazin-1-ylalkyl, 4- $[\text{C}_6$  or  $\text{C}_{10}]$ arylpiperidin-1-ylalkyl, azetidin-1-ylalkyl, morpholin-4-ylalkyl, thiomorpholin-4-ylalkyl, piperidin-1-ylalkyl,  $[\text{C}_6$  or  $\text{C}_{10}]$ aryl, or independently the same as  $\text{R}^6$ ;
  - 25 (b)  $\text{R}^6$  is phenyl substituted on the para position with chloro or fluoro;
- c. X is a pharmaceutically acceptable anion, or
- (B) a pharmaceutically acceptable salt of the compound,
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wherein aryl (including phenyl) or Ar<sup>4</sup> can be substituted with, in addition to any substitutions specifically noted, one or more general substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, Ar<sup>4</sup>C(O)-, Ar<sup>4</sup>C(O)NH-, Ar<sup>4</sup>O-, Ar<sup>4</sup>-, Ar<sup>4</sup>-alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl; and

wherein heterocycles, except those of Ar<sup>4</sup>, can be substituted with, in addition to any substitutions specifically noted, the following general substitutions: acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, Ar<sup>4</sup>C(O)-, Ar<sup>4</sup>O-, Ar<sup>4</sup>-, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

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- 20 The compound of Claim 36, wherein an adjacent pair from R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup>, together with their ring carbons, form a C<sub>6</sub>- or C<sub>10</sub>- aromatic fused ring which can be substituted by one or more halo, amino, alkyl, sulfonic acid, alkylsulfonyl or ω-alkylenesulfonic acid groups, or a C<sub>1</sub>-C<sub>3</sub> alkylenedioxy group.

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- 25 The compound of claim 36, wherein  
a. R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup>

1. are independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, allyl, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, halo, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, Ar<sup>4</sup>, Ar<sup>4</sup>-alkyl, Ar<sup>4</sup>-O, Ar<sup>4</sup>SO<sub>2</sub>-, Ar<sup>4</sup>SO-, Ar<sup>4</sup>S-, Ar<sup>4</sup>SO<sub>2</sub>NH-, Ar<sup>4</sup>NH, (N-Ar<sup>4</sup>)(N-



alkyl)N-, Ar<sup>4</sup>C(O)-, Ar<sup>4</sup>C(O)NH-, Ar<sup>4</sup>NH-C(O)-, and (N-Ar<sup>4</sup>)(N-alkyl)N-C(O)-;  
or

2. form, with an adjacent pair from R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup>, together with their ring carbons, a C<sub>6</sub>- or C<sub>10</sub>- aromatic fused ring system; or
- 5 3. form, with an adjacent pair from R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup>, together with their ring carbons, a C<sub>5</sub>-C<sub>7</sub> fused cycloalkyl ring; or
4. form, with an adjacent pair from R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup>, together with their ring carbons, a 5- or 6-membered heteroaryl ring, wherein each heteroaryl ring may, in addition to the general substitutions, be optionally substituted with one or more halo or
- 10 (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy groups; or
5. form, with an adjacent pair from R<sup>17</sup>, R<sup>18</sup> and R<sup>19</sup>, together with their ring carbons, a five to eight membered heterocycle; and
- c. X is a pharmaceutically acceptable anion, or
- (B) a pharmaceutically acceptable salt of the compound,
- 15 wherein aryl or Ar<sup>4</sup> can be substituted with, in addition to any substitutions specifically noted, one or more substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, Ar<sup>4</sup>C(O)-, Ar<sup>4</sup>C(O)NH-, Ar<sup>4</sup>O-, Ar<sup>4</sup>-,
- 20 Ar<sup>4</sup>-alkyl-, carboxy, carboxyalkyl, cycloalkyl, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid;
- wherein heterocycles, except those of Ar<sup>4</sup>, can be substituted with, in addition to any substitutions specifically noted, acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylsulfonyl, alkylsulfinyl, alkylthio, Ar<sup>4</sup>C(O)-,
- 25 Ar<sup>4</sup>O-, Ar<sup>4</sup>-, carboxy, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

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40. The compound of claim 39, wherein if Y has a core structure of phenyl substituted at the para position with chloro, then the compound of formula VIII differs from a salt of 1-[2-(4-bromophenyl)-2-oxoethyl]-5-cyano-pyrimidinium by a substitution difference of more than the cyano (which is not within the scope of R<sup>18</sup>).

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41. The compound of claim 39, wherein Y<sup>2</sup> is according to formula -CH(R<sup>5</sup>)-W-Rs.



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42.

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A compound of claim 36 selected from:

1-(4-Fluoro-benzyl)-pyrimidin-1-ium bromide; and

1-(4-Chloro-benzyl)-pyrimidin-1-ium chloride.

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A pharmaceutical composition comprising:

a compound of one of claims 36 to 42; and

a pharmaceutically acceptable excipient.

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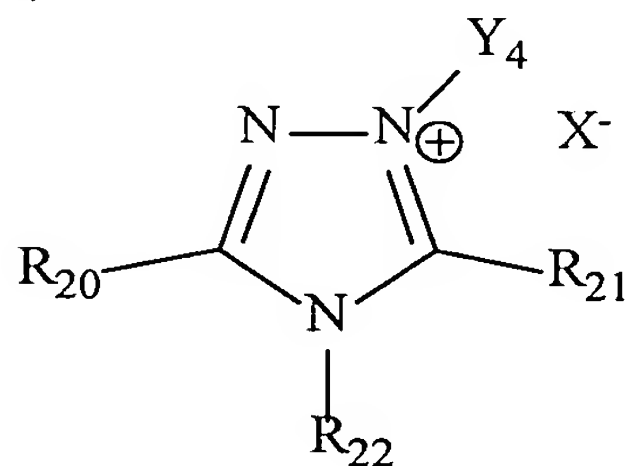
A method of treating an indication of the invention with a pharmaceutically effective amount of a compound of one of claims 36 to 42.

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A compound of formula IX:



(IX)

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wherein

- a. one of  $R^{20}$  and  $R^{21}$  is hydrogen, and the other is selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino,  $(C_1-C_3)$ alkylenedioxy, allyl, amino,  $\omega$ -alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, hydroxy,  $(C_2-C_6)$ hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, 4- $[C_6 \text{ or } C_{10}]$ aryl piperidin-1-yl, 4- $[C_6 \text{ or } C_{10}]$ aryl piperazin-1-yl,  $Ar^5$  (wherein  $Ar^2$  is  $C_6$  or  $C_{10}$  aryl),  $Ar^5$ -alkyl,  $Ar^5$ -O-,  $Ar^5SO_2$ -,  $Ar^5SO$ -,  $Ar^5S$ -,  $Ar^5SO_2NH$ -,  $Ar^5NH$ -,  $(N-Ar^5)(N-alkyl)N$ -,  $Ar^5C(O)$ -,  $Ar^5C(O)NH$ -,  $Ar^5NH-C(O)$ -, or  $(N-Ar^5)(N-alkyl)N-C(O)$ -;
- b.  $R^{22}$  is acylamino, acyloxyalkyl, alkanoylalkyl, alkenyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, allyl, carbamoyl, carboxyalkyl, dialkylamino,  $(C_2$ -

C<sub>6</sub>)hydroxyalkyl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl, Ar<sup>5</sup>, Ar<sup>5</sup>-alkyl, Ar<sup>5</sup>-O, Ar<sup>5</sup>SO<sub>2</sub>-, Ar<sup>5</sup>SO-, Ar<sup>5</sup>S-, Ar<sup>5</sup>SO<sub>2</sub>NH-, Ar<sup>5</sup>NH, (N-Ar<sup>5</sup>)(N-alkyl)N-, Ar<sup>5</sup>C(O)-, Ar<sup>5</sup>C(O)NH-, Ar<sup>5</sup>NH-C(O)-, or (N-Ar<sup>5</sup>)(N-alkyl)N-C(O)-;

5 c. Y<sup>4</sup> is a group of the formula -CH(R<sup>5</sup>)-R<sup>6</sup> wherein

(a) R<sup>5</sup> is hydrogen, alkyl-, cycloalkyl-, alkenyl-, alkynyl-, aminoalkyl-, dialkylaminoalkyl-, (N-[C<sub>6</sub> or C<sub>10</sub>]aryl)(N-alkyl)aminoalkyl-, piperidin-1-ylalkyl-, 1-pyrrolidinylalkyl, azetidylalkyl, 4-alkylpiperazin-1-ylalkyl, 4-alkylpiperidin-1-ylalkyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-ylalkyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-ylalkyl, azetidin-1-ylalkyl, morpholin-4-ylalkyl, thiomorpholin-4-ylalkyl, piperidin-1-ylalkyl, [C<sub>6</sub> or C<sub>10</sub>]aryl, or independently the same as R<sup>6</sup>;

(b) R<sup>6</sup> is

(1) cyano;

15 (2) a group of the formula -W-Rs, wherein W is -C(=O)- or -S(O)<sub>n</sub>- where n=1 or 2, and wherein Rs is a [C<sub>6</sub> or C<sub>10</sub>]aryl or a heterocycle containing 4-10 ring atoms of which 1-3 are heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur; and

d. X is a pharmaceutically acceptable anion, or

20 (B) a pharmaceutically acceptable salt of the compound,

wherein aryl or Ar<sup>5</sup> can be substituted with, in addition to any substitutions specifically noted, one or more general substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylamino, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, Ar<sup>5</sup>C(O)-, Ar<sup>5</sup>C(O)NH-, Ar<sup>5</sup>O-, Ar<sup>5</sup>-, Ar<sup>5</sup>-alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl; and

wherein heterocycles, except those of Ar<sup>5</sup>, can be substituted with, in addition to any substitutions specifically noted, the following general substitutions: acylamino, alkanoyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylamino,

alkylsulfonyl, alkylsulfinyl, alkylthio, amino,  $\text{Ar}^5\text{C}(\text{O})-$ ,  $\text{Ar}^5\text{O}-$ ,  $\text{Ar}^5-$ , carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

5 <sup>45</sup>  
~~46~~ <sup>^</sup> The compound of claim 45, wherein  $\text{Y}^4$  is according to formula  $-\text{CH}(\text{R}^5)-\text{W}-\text{Rs}$ .

<sup>46</sup>  
~~47~~ <sup>^</sup> The compound of Claim 45, wherein

a.  $\text{R}^{20}$  and  $\text{R}^{21}$  are independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl,  $(\text{C}_1-\text{C}_3)$ alkylenedioxy, allyl,  $\omega$ -alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, halo, hydroxy,  $(\text{C}_2-\text{C}_6)$ hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl,  $\text{Ar}^2$ ,  $\text{Ar}^2$ -alkyl,  $\text{Ar}^2-\text{O}$ ,  $\text{Ar}^2\text{SO}_2-$ ,  $\text{Ar}^2\text{SO}-$ ,  $\text{Ar}^2\text{S}-$ ,  $\text{Ar}^2\text{SO}_2\text{NH}-$ ,  $\text{Ar}^2\text{NH}$ ,  $(\text{N}-\text{Ar}^2)(\text{N}-\text{alkyl})\text{N}-$ ,  $\text{Ar}^2\text{C}(\text{O})-$ ,  $\text{Ar}^2\text{C}(\text{O})\text{NH}-$ ,  $\text{Ar}^2\text{NH}-\text{C}(\text{O})-$ , and  $(\text{N}-\text{Ar}^2)(\text{N}-\text{alkyl})\text{N}-\text{C}(\text{O})-$ ;  
10  
15 or

b. Y is a group of the formula  $-\text{CH}(\text{R}^5)-\text{R}^6$  wherein

(a)  $\text{R}^5$  is hydrogen or alkyl;

(b)  $\text{R}^6$  is

(1) cyano;

20 (2) a group of the formula  $-\text{W}-\text{Rs}$ , wherein W is  $-\text{C}(=\text{O})-$  or  $-\text{S}(\text{O})_n-$  where  $n=1$  or 2; and

g. X is a pharmaceutically acceptable anion, or

(B) a pharmaceutically acceptable salt of the compound,

wherein aryl or  $\text{Ar}^2$  can be substituted with, in addition to any substitutions specifically

25 noted, one or more general substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl,  $(\text{C}_1-\text{C}_3)$ alkylenedioxy, alkylsulfonyl, alkylsulfinyl,  $\omega$ -alkylenesulfonic acid, alkylthio, allyl,  $\text{Ar}^2\text{C}(\text{O})-$ ,  $\text{Ar}^2\text{C}(\text{O})\text{NH}-$ ,  $\text{Ar}^2\text{O}-$ ,  $\text{Ar}^2-$ ,  $\text{Ar}^2$ -alkyl-, carboxy, carboxyalkyl, cycloalkyl, halo, trifluoromethyl, hydroxy,  $(\text{C}_2-\text{C}_6)$ hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid; and  
30 wherein heterocycles, except those of  $\text{Ar}^2$ , can be substituted with, in addition to any substitutions specifically noted, the following general substitutions: acylamino,

alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylsulfonyl, alkylsulfinyl, alkylthio,  $\text{Ar}^2\text{C}(\text{O})-$ ,  $\text{Ar}^2\text{O}-$ ,  $\text{Ar}^2-$ , carboxy, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

5 <sup>47</sup>  
~~48.~~ The compound of claim 47, wherein  $\text{Y}^*$  is according to formula  $-\text{CH}(\text{R}^5)-\text{W}-\text{Rs}$ .  
^

<sup>48</sup>  
~~49.~~ A pharmaceutical composition comprising:  
^  
a compound of one of claims 45 to 48; and  
a pharmaceutically acceptable excipient.

10 <sup>49</sup>  
~~50.~~ A method of treating an indication of the invention with a pharmaceutically  
^  
effective amount of a compound of one of claims 45 to 48.